UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/756,983 | 01/09/2001 | Salvatore Albani | 031544.0004.CIP | 6818 |

23865 7590 01/10/2003

BROBECK, PHLEGER & HARRISON LLP
12390 EL CAMINO REAL
SAN DIEGO, CA 92130

| EXAMINER |
|---|
| EWOLDT, GERALD R |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

DATE MAILED: 01/10/2003 10

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/756,983 | Applicant(s) Albani |
|---|---|---|
| | Examiner G.R. Ewoldt | Art Unit 1644 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *11/13/01 and 10/30/02*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above, claim(s) *4, 5, 9, and 11* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3, 6-8, and 10* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Nov 13, 2001* is/are a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *1.5*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Form 206*

**UNITED STATES DEPARTMENT OF COMMERCE**
**Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

09/756983

| SERIAL NUMBER | FILING DATE | FIRST NAMED APPLICANT | ATTORNEY DOCKET NO. |
|---|---|---|---|
| | | | |

| EXAMINER | |
|---|---|
| | |
| ART UNIT | PAPER NUMBER |
| | 10 |

DATE MAILED:

The decision on the petition filed in the above entitled application is as follows:

☐ Delay in Prosecution Held Unavoidable (35 U.S.C. 133),

Petition Granted _____

☐ Delayed Payment of Issue Fee Accepted (35 U.S.C. 151),

Petition Granted _____

☐ Petition Granted _____

☒ Petition Denied The petition filed 4/2/02 requesting acceptance of color drawings under 37 CFR 1.84 is hereby denied. Although 3 sets of color drawings were submitted, the specification on page 1 has not been amended to disclose the following information: "The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawings will be provided by the Patent and Trademark Office upon request and payment of the necessary fee".

☐ Petition Dismissed _____

By direction of the Deputy
Assistant Commissioner for Patents

Christina Chan
CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

**DETAILED ACTION**

1. Applicant's election with traverse of Group I, Claims 1-3 and 5, in Paper No. 9, filed 10/30/02, is acknowledged. Applicant's traversal is on the grounds that because independent Claims 1 and 6 recite the word "comprising", all claims should be examined together. Applicant further argues that "If such practice was not allowed, each patent would necessarily contain but one claim." Applicant further argues that the examiner has made no *prima facie* case showing a serious search burden.

These arguments not found persuasive for the following reasons. Regarding the use of the term "comprising", said use alone is insufficient to require the examination of multiple inventions in a single application. If said use were sufficient, Applicant would need only glue multiple inventions together using "comprising" to avoid restriction altogether. Regarding the assertion that restriction would necessarily lead to single claim applications, it is clear that in the instant case multiple claims are under examination, thus, the assertion cannot be true. Regarding search burden, while it has been noted that the Groups are classified in the same class and subclass, in the establishment of search burden, classification of subject matter is merely one indication of the burdensome nature of the search involved. In the biotechnological arts, the literature searches are generally far more important in evaluating burden of search. In the instant application, the claimed inventions consist of different components, e.g., whereas the invention of Group II includes co-stimulator molecules, the invention of Group III does not. Clearly then, different searches and different issues are involved in the examination of each group, thus search burden has been established.

Upon reconsideration, however, Group V has been rejoined with Group I as the invention of Group V consists of no additional active components but rather only a specific linking molecule.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 4, 5, 9, and 11 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-3, 6-8, and 10 are being acted upon.

3. Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied. Note that while a petition under 37 CFR 1.84(a)(2)has been filed, and the fee paid, the required amendment to the specification has not been filed.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-3, 6-8, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically:

A) The term "GM-1" has not been defined in the specification. Accordingly, said term is vague and indefinite. Applicant is advised that amending "GM-1" to "GM-1 ganglioside" would obviate the rejection.

B) The phrases "cholera toxin β subunit associated with a GM-1 molecule," or "MHC component is associated with the cholera toxin β subunit," are considered vague and indefinite as the term "associated with" has no specific definition within the context in which it is being used. Applicant is advised that amending "associated with" to "bound to" would obviate the rejection.

C) The phrase "immunologically active MHC component" is considered vague and indefinite as the term "immunologically active" has not been defined and has no specific definition in the art.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3, 6-8, and 10 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) The phrases "cholera toxin β subunit associated with a GM-1 molecule," or "MHC component is associated with the cholera toxin β subunit".

B) The phrase "at least a portion of a cholera toxin β subunit associated with a GM-1 molecule".

Applicant's amendment, filed 10/30/02, fails to assert that no new matter has been added and no specific support for the changes has found in the specification.

8. Claims 1-3, 6-8, and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

an artificial APC comprising a phosphotidylcholine and cholesterol liposome of 2 parts cholesterol to 7 parts phosphotidylcholine, said liposome further comprising a GM-1 ganglioside bound to a cholera toxin β subunit, said cholera toxin β subunit further being bound to a MHC-antigenic peptide complex in an orientation such that the MHC-antigen complex faces outward on the artificial APC,

does not reasonably provide enablement for:

an artificial APC comprising a liposome, and at least one GM-1 associated with a cholera toxin β subunit, and a n immunologically active MHC component associated with said cholera toxin β subunit.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the

claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

The invention of the instant claims is drawn to an artificial APC comprising a liposome, said liposome further comprising a GM-1 ganglioside, a cholera toxin β subunit, and an antigen-loaded MHC molecule.

Liposomes comprising MHC molecules for antigen presentation are well-known in the art, see for example Walden et al., 1985. The specification discloses that the artificial APCs of the instant claims are distinct from the liposomes comprising MHC molecules of the prior art in two ways. First, the specific lipids used, and second, the use of the GM-1 ganglioside - cholera toxin β subunit complex to orient the molecules of interest towards the outside of the artificial APC.

Regarding the lipids used in the instant invention, the specification discloses at page 15 that "the MHC:antigen:accessory molecule complexes in conjunction with other functional molecules are able to migrate in proper orientation in the lipid bilayer of the liposome because of the use of a unique combination of lipids and surfactant molecules, namely an optimal ratio of phosphotidylcholine and cholesterol." Clearly then, any known liposome cannot function in the artificial APC of the instant claims. The specification further discloses that the artificial APCs of the instant claims require the use of neutral lipids whereas most of the liposomes of the prior art employ charged lipids. Note that the specification provides just one working example of the claimed liposome consisting of phosphotidylcholine and cholesterol mixed at a 7:2 ratio. Accordingly, given the breadth of the claims encompassing any and all possible liposomes, an artificial APC comprising charged lipids, or neutral lipid to cholesterol ratios other than 7:2, would be considered highly unpredictable and unlikely to function as set forth in the specification. As such, said artificial APCs would require undue experimentation to use.

Regarding the requirement that the GM-1 ganglioside be bound to a cholera toxin β subunit, and that the cholera toxin β subunit further be bound to a MHC-antigenic peptide complex in an orientation such that the MHC-antigen complex faces outward on the artificial APC, the specification discloses that this binding is what achieves the unique feature of the artificial APC of the

instant claims, i.e., the greater-than-random orienting of the MHC-antigen complexes towards the surface of the artificial APC which allows for T cell capping, which in turn activates T cells. As currently set forth, the claims merely require that all the claimed components be present in an undefined fashion. Accordingly, the product of the random "association" of the claimed components would be considered highly unpredictable and requiring of undue experimentation for use as an artificial APC.

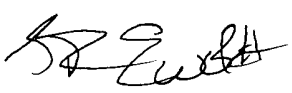
*In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient working examples encompassing the breadth of the claimed invention, the unpredictability of the art, and the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

9. No claim is allowed.

10. The Form 1449, filed 1/09/01, has not been initialed as none of the references have been received by the Examiner.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday and alternate Fridays from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The CM1 Fax Center telephone numbers are 703-872-9306 (before final) and 703-872-9307 (after final).



G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
January 10, 2003